Unraveling the Impact of Education on Cognitive Resilience in Dementia: A Longitudinal Mixed-Effects Analysis

Introduction:

In the landscape of medical research, neurodegenerative diseases such as dementia stand as towering challenges of our age. Understanding dementia, characterized by the decline in memory, language, problem-solving, and other thinking skills that affects a person's ability to perform everyday activities, is not just a medical necessity but a societal imperative. In this study, we delve into a rich dataset derived from a longitudinal study on magnetic resonance imaging (MRI) results of patients diagnosed with dementia, juxtaposed against control subjects without the condition. The MRI results, accompanied by socio-demographic data and clinical assessments, offer a window into the intricate narrative of cognitive decline.

Research Questions:

Guided by the preliminary exploratory data analysis, the study pivots around pivotal research questions that seek to unravel the associations and patterns within this dataset:

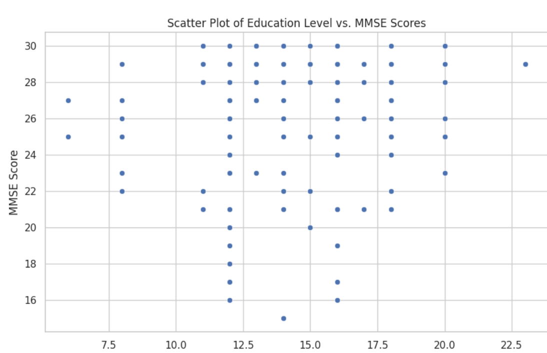
1. ***Does the level of education (EDUC) influence the rate of cognitive decline, as measured by Mini-Mental State Examination (MMSE) scores, in patients diagnosed with dementia?***

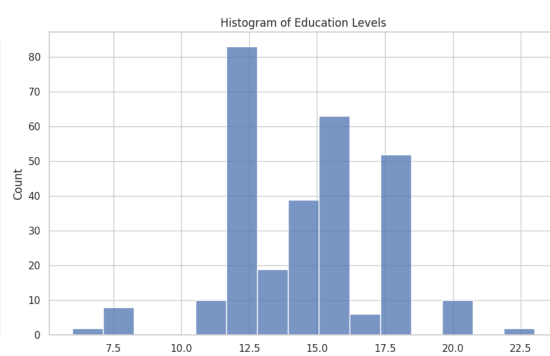
2. ***Are there observable and statistically significant differences in brain volume, particularly normalized whole brain volume (nWBV), across subsequent visits, that correlate with the progression of dementia?***

Exploratory Data Analysis (EDA):

Before diving into the intricacies of mixed-effects models, an initial foray into the dataset through exploratory data analysis (EDA) sets the stage for a more targeted inquiry. The EDA focused on variables of central interest to our research questions: education level (EDUC), cognitive function as measured by the Mini-Mental State Examination (MMSE), and brain volume, particularly normalized whole brain volume (nWBV).

Education and Cognitive Function:

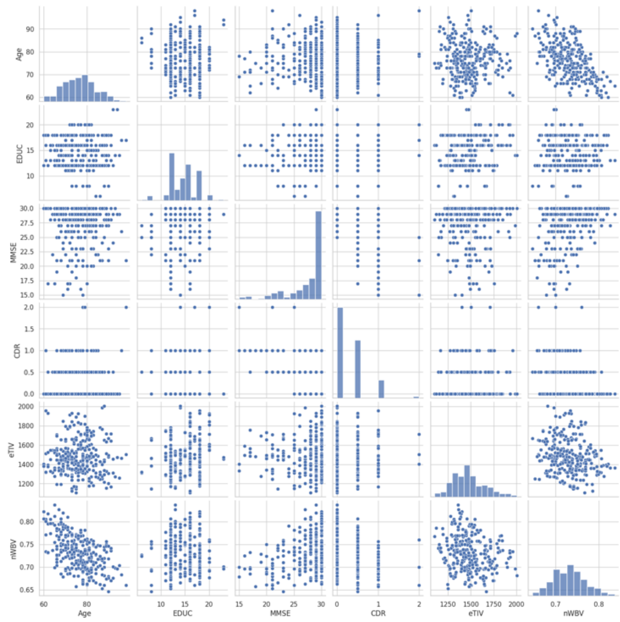




- A preliminary examination of the dataset revealed a spectrum of educational backgrounds among the participants. Histograms indicated a range from 6 to over 20 years of education, with the majority clustered around 12 to 16 years.

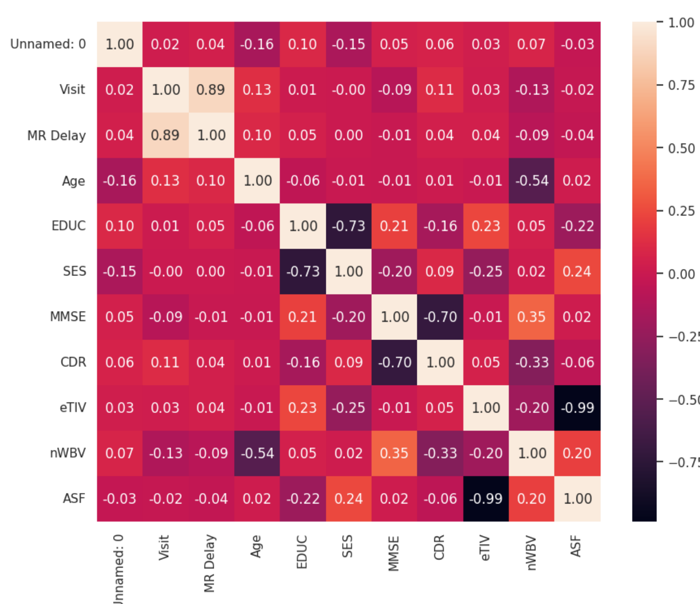
- Plotting education level against MMSE scores did not immediately reveal a straightforward relationship; however, a nuanced pattern suggests that higher education levels might be associated with higher MMSE scores, potentially indicating better cognitive function.

Brain Volume and Dementia:



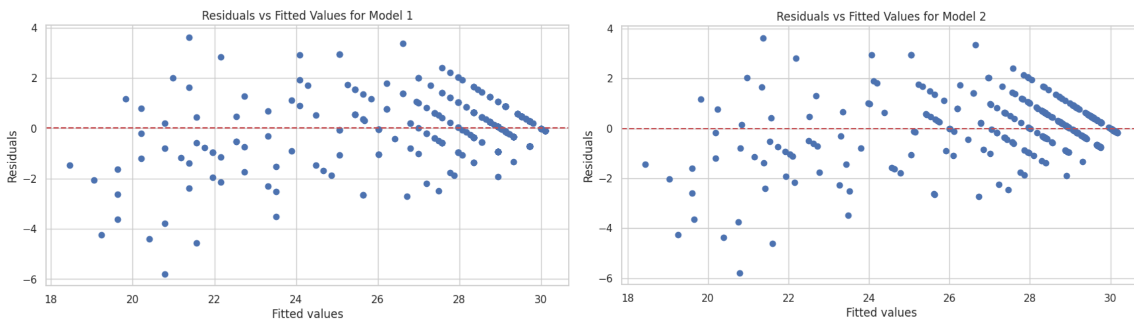
Assessing brain volume through MRI, particularly the nWBV, showed variations across the sample. Successive scans for individuals allowed for an initial understanding of brain volume changes over time.the data hinted at a trend where individuals diagnosed with dementia exhibited a decline in nWBV across visits, which could suggest progressive atrophy associated with the disease.

Correlations and Patterns:



- A correlation matrix was employed to discern relationships between all variables at a glance. Notably, a moderate negative correlation was detected between MMSE and CDR, reaffirming the established inverse relationship between cognitive function and dementia severity.
- Age distribution across dementia groups was inspected to rule out age as a confounding factor in subsequent analyses. The relatively uniform distribution of ages across the groups supported the decision to focus on educational and brain volume factors.

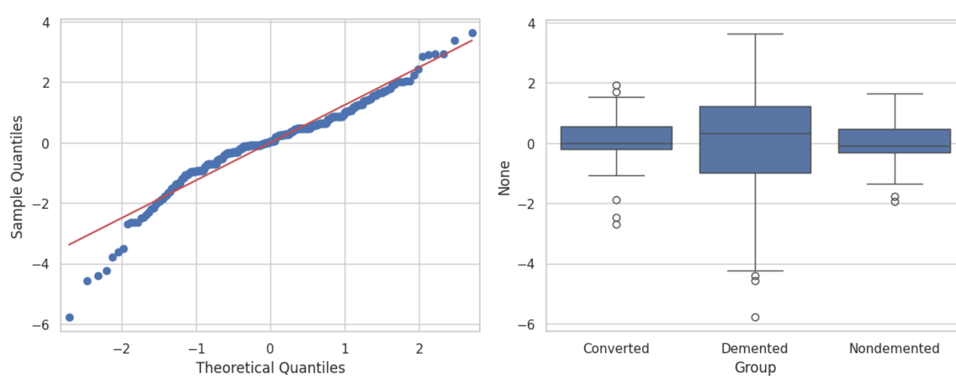
Mixed-Effects ANOVA Insights and Assumption Checks:



Upon the application of mixed-effects ANOVA to our dataset, we gleaned insights into the cognitive trajectory of dementia patients vis-à-vis their educational background and group classification. The model's coefficients shed light on the dynamics influencing Mini-Mental State Examination (MMSE) scores. Interestingly, the analysis revealed that being classified within the **Demented** group was significantly associated with a decrease in MMSE scores, pointing to the detrimental impact of dementia on cognitive functioning. Conversely, the **Nondemented** group did not show a significant deviation from the baseline, indicating a stable cognitive profile.

The effect of the second visit (**Visit**) on MMSE scores was significant, suggesting a notable change in cognitive function between the two visits. This aligns with the progressive nature of dementia, where cognitive decline can be expected as time progresses. Meanwhile, the roles of age and education (**EDUC**) presented a more nuanced picture, as their coefficients, while indicative of a trend, did not achieve statistical significance within this model. This implies that the effect of education on cognitive function, as captured by MMSE, might be subtle or overshadowed by the stronger effects of dementia pathology.

Normality check and homogeneity check for model 1



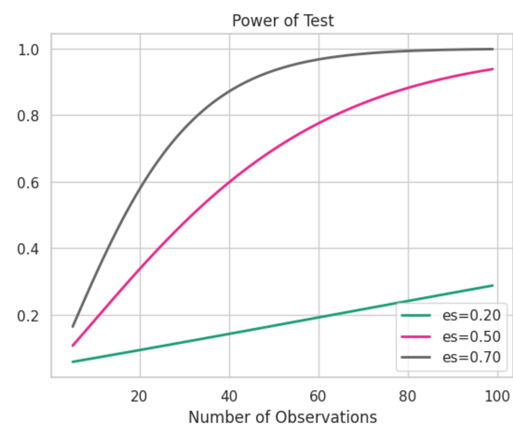
Normality check and homogeneity check for model 2 please refer to the notebook

Diligent examination of the model's assumptions through diagnostic plots has unveiled areas warranting cautious interpretation. The residuals versus fitted values plots illustrated a fan-shaped pattern, raising the specter of heteroscedasticity, where the variance of errors is not consistent across the spectrum of fitted values. Such patterns suggest the need for potential model adjustments or the adoption of heteroscedasticity-consistent standard errors.

In the Q-Q plots, the alignment of data points with the theoretical line in the central quantiles corroborated the assumption of normality in the middle range of the distribution. However, some divergence at the tails was noted, indicating that extreme values may not align perfectly with a normal distribution. This could be a reflection of outliers or an indication of a non-normal distribution in the extremities.

Furthermore, the boxplots across the different dementia groups displayed a variance in residuals that may not be entirely homogeneous, suggesting that the experiences of cognitive decline are not uniform across the spectrum of dementia and may interact with other unidentified factors.

Statistical Power Analysis:



In preparation for further experimental design, a statistical power analysis was conducted to determine the necessary sample size to detect an effect size of 0.7 with a power of 0.91 and an alpha of 0.05. The analysis suggested that a sample size of approximately 46 participants would be required to achieve these parameters. The accompanying power curve graphically illustrates the relationship between sample size and the likelihood of detecting true effects, underscoring the importance of adequate sample sizing in research design.

Conclusion and Reflections:

In conclusion, this study's mixed-effects ANOVA provided valuable insights into the influence of dementia on cognitive function over time and the non-significant yet potentially interesting role of education. Although the analysis faced limitations, such as assumption violations that necessitate cautious interpretation, it serves as a springboard for future research. The statistical power analysis underscored the need for careful planning in subsequent studies to ensure robust and reliable findings. This research journey illuminates the complex interplay of education, aging, and dementia and sets the stage for continued exploration into the factors that contribute to cognitive resilience.